



UNITED STATES PATENT AND TRADEMARK OFFICE

[Handwritten signature]

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/702,039 | 11/06/2003 | Bernhard Nicswandt | 06478.1478-01000 | 7427 |

7590 11/17/2004

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

| |
|----------|
| EXAMINER |
|----------|

HADDAD, MAHER M

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1644

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/702,039

Applicant(s)

NIESWANDT, BERNHARD

Examiner

Maher M. Haddad

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2004.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
4a) Of the above claim(s) 7 and 8 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-6 and 9-13 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 10/051,168.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 11/4/03.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-13 are pending.
2. Applicant's election with traverse of Group I, claims 1-6 and 9-13 drawn to a medicament for protection against thrombotic diseases as it reads on an antibody JAQ1 and a hybridoma and a method of producing filed on 10/19/04, is acknowledged.

Applicant's traversal is on the grounds that the it would not be an undue burden on the Office to search the art concerning Groups I and II at one time. Applicant submits that Group II includes only 2 claims, both containing a high degree of subject matter overlap with Group I. Applicant contends that searching the art concerning Group II, in which antibody JAQ1 is fixed to a solid carrier, would be encompassed in the search for antibody JAQ1 generally. Applicant concluded that it would not add to the Office's burden to search both groups together. This is not found persuasive because the JAQ1 antibody and a method using the antibody are distinct. Group I and II have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter. Therefore restriction for examination purposes as indicated is proper. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 7-8 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.
4. Claims 1-6 and 9-13 are under examination as they read on a medicament for protection against thrombotic diseases as it reads on an antibody JAQ1 and a hybridoma and a method of producing.
5. Applicant's IDS, filed 11/04/03, is acknowledged.
6. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title".

Claims 11-13 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Art Unit: 1644

7. Claims 1-6 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- A) Claims 1-5 and 11-13 are indefinite in the recitation of "active principle" since a principle is not an art recognize term and further the phrase refers to a chemical ingredient rather than a biological ingredient that exhibits or imparts a characteristic quality.
- B) Claim 1, line 3 is indefinite in the recitation of "degradation" it is unclear as how the active principle would degrade the collagen receptor and whether the active principle has an proteolytic activity.
- C) Claims 3, 5, 10 and 13-14 are indefinite in the recitation of "JAQ1" because its characteristics are not known. The use of "JAQ1" monoclonal antibody as the sole means of identifying the claimed antibody and hybridoma renders the claim indefinite because "JAQ1" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct hybridomas or cell lines. It is suggested that the DSM ACC 2487 be cited in the claims.
- D) Claims 11-13 provide for the use of the active principle that induces an irreversible inactivation or degradation of collagen receptor on thrombocytes, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
- E) It is improper to recite "Monoclonal antibody" in claim 10, line 1. It is suggested that the article "A" should be inserted before the phrase.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-6 and 9-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

Art Unit: 1644

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the **hybridoma DSM ACC 2487 that produce the JAQ1 antibody**, recited in claims 3, 5-6, 9-10 and 13, is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridoma, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806.

Further, amendment of the specification to disclose the date of deposit and the complete address of the depository is required as set forth in 37 C.F.R. 1.809(d).

Further the specification does not reasonably provide enablement for **any medicament for protection against thrombotic diseases characterized in that it comprises at least one active principle that induces an irreversible inactivation or degradation of any collagen receptor on thrombocytes** in claim 1; which characterized in that an antibody induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes in claim 2, characterized in that it comprises the monoclonal antibody JAQ1 in claim 3, characterized in that it contains an antibody against the thrombocyte collagen receptor GPVI in claim 4, characterized in that it contains the humanized monoclonal antibody JAQ1 in claim 5, or a diagnostic agent for the determination of the expression rate of the collagen receptor GPVI, characterized in that it contains a labeled monoclonal or polyclonal antibody directed against the GPVI epitope, preferably as defined by JAQ1 in claim 6, or a monoclonal antibody, characterized in that it binds to the "same or similar epitope of the collagen receptor" for thrombocytes as the monoclonal antibody JAQ1 in claim 10, use of the active principle that induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes for the preparation of a medicament against thrombotic diseases in claim 11, wherein the active principle is a monoclonal antibody in claim 12, wherein the active principle is the monoclonal antibody JAQ1 in claim 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use medicaments comprising “at least active principle” that induces an irreversible inactivation or degradation of any “collagen receptor on thrombocytes”, wherein the at least one active principle is “any antibody”; any monoclonal antibody that binds to the same or a similar epitope of any “collagen receptor” for thrombocytes as monoclonal antibody JAQ1.

Applicant has not provided sufficient biochemical information that distinctly identifies such “active principle” other than monoclonal JAQ1 antibody against GPVI. While any “active principle” may have some notion of the activity of the “inducing agent”, claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such active principles, commensurate in scope with the claimed invention. The specification (page 5 under Antibodies, lines 5-19) fails to provide any guidance on how to make any medicament, any antibody, any collagen receptor, any GPVI epitope, or any monoclonal antibody or any polyclonal antibody that can be used to use to induce an irreversible inactivation or degradation of collagen receptor GPVI on thrombocytes.

Regarding collagen receptor, Schulte et al (J Biol Chem. 2001 Jan 5; 276(1):364-368, IDS ref. C2) have shown that JAQ1 is unable to inhibit activation of platelets by high concentrations of collagen, suggesting the presence of a second, GPVI-independent collagen receptor (see abstract in particular). The specification fails to provide guidance as to which collagen receptor is irreversibly inactivated or degraded, neither does the specification disclose which collagen receptor the claimed antibody binds. Further, the specification lack guidance regarding the collagen receptor epitope. Because of this lack of guidance, an undue experimentation would be required to determine which collagen receptor would lead to an irreversible inactivation or degradation of a collagen receptor on thrombocytes.

Further, there is insufficient guidance as to which amino acid epitopes within the collagen receptor GPVI can be unique and induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since no epitope of a collagen receptor is mapped or provided, an undue experimentation would be required to determine the epitope and any antibody that binds to the same or similar epitope of the collagen receptor.

Also, at issue is whether or not the claimed medicament would function to protect “against thrombotic diseases”. The specification discloses the treatment with monoclonal antibody JAQ1 resulted in profound long-term antithrombotic protection against collagen-dependent thromboembolism. The exemplification is drawn to the depletion of an activating glycoprotein receptor from circulation platelets, in a model of lethal pulmonary thromboembolism induced by infusion of a mixture of collagen and epinephrine (page 11).

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since mice animals were used as model

Art Unit: 1644

system to protect against thrombotic disease. It is not clear that reliance on a model of lethal pulmonary thromboembolism induced by infusion of a mixture of collagen and epinephrine accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively reach any therapeutic endpoint in mammals by administering the therapeutic medicament. The specification does not teach how to extrapolate data obtained from a mice model of lethal pulmonary thromboembolism studies to the development of effective in vivo mammalian therapeutic protection, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the medicament exemplified in the specification.

However, an effective protocol for the protection against thrombotic diseases in mammalian is subject to a number of factors which enter the picture beyond simply the administration of the medicament in an acceptable formulation. Demonstrating depletion of an activating glycoprotein receptor from circulation platelets cannot alone support the predictability of the method for protection against thrombotic diseases through administration of the appropriate formulation. The ability of a host to suppress and thereby protect against thrombotic diseases will vary depending upon factors such as the condition of the host and burden of disease.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 1-6 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of anti-GPVI antibody and JAQ1 antibody which specifically binds GPVI for diagnostic assays.

Applicant is not in possession of any medicament for protection against thrombotic diseases characterized in that it comprises at least one active principle that induces an irreversible inactivation or degradation of any collagen receptor on thrombocytes in claim 1; which characterized in that an antibody induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes in claim 2, characterized in that it comprises the monoclonal antibody JAQ1 in claim 3, characterized in that it contains an antibody against the thrombocyte collagen receptor GPVI in claim 4, characterized in that it contains the humanized monoclonal antibody JAQ1 in claim 5, or a diagnostic agent for the determination of the expression rate of the collagen receptor GPVI, characterized in that it contains a labeled monoclonal or polyclonal antibody directed against the GPVI epitope, preferably as defined by JAQ1 in claim 6, or a monoclonal antibody, characterized in that it binds to the "same or similar epitope of the

Art Unit: 1644

collagen receptor" for thrombocytes as the monoclonal antibody JAQ1 in claim 10, use of the active principle that induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes for the preparation of a medicament against thrombotic diseases in claim 11, wherein the active principle is a monoclonal antibody in claim 12, wherein the active principle is the monoclonal antibody JAQ1 in claim 13.

Applicant has disclosed only anti-GPVI and JAQ1 antibody which specifically binds to collagen receptor; therefore, the skilled artisan cannot envision all the contemplated antibodies possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Art Unit: 1644

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 1-4 and 9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Nieswandt *et al* (IDS ref No. C5) (J Biol Chem. 275(31):23998-4002, 2000).

Nieswandt *et al* teach a medicament comprising a monoclonal antibody against the platelet collagen receptor glycoprotein GPVI (JAQ1) which inhibited collagen-induced platelet aggregation (see abstract and page 23400, right column, 2nd paragraph in particular). Finally Nieswandt *et al* teach a method for producing a monoclonal antibody and a hybridoma cell line for the production of the monoclonal antibody wherein the antibody is the monoclonal antibody JAQ1 (page 23999 under Production of Monoclonal antibodies in particular). Further, Nieswandt *et al* teach the JAQ1 antibody in a composition e.g 20 µg/ml and 10 µg/ml (see figures 1-4, in particular). While the prior art teachings may be silent as to the “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” per se; the antibody used in the reference is the same as the claimed antibody. Therefore “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” is considered inherent properties.

When a claim recites using an old composition or structure (e.g. JAQ1 monoclonal antibody) and the use is directed to a result or property of that composition or structure (the protection against thrombotic diseases characterized in that it comprises an active principle that induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The reference teachings anticipate the claimed invention.

14. Claims 1-2, 4 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Clemetson *et al* (IDS ref No. C3) (J Biol Chem. 274(41):29019-24, 1999), as is evidenced by Schulte *et al* (Blood, 15 May 2003, Vol. 101, No. 10, pp. 3948-3952).

Clemetson *et al* teach a medicament, comprising polyclonal antibodies fragment Fab against human platelet collagen receptor GPVI, which inhibited collagen-induced platelet aggregation (see abstract page 29019 and page 29021 1st paragraph in particular). Furthermore, Clemetson *et al* teach a method of producing the medicament, comprising preparing the polyclonal antibodies against human GPVI in rabbits and preparing Fab fragments using standard protocol (see page 29020 under Preparation of anti-GPVI Fab and Fa(ab')₂ in particular). Clemetson *et al* teach that antibody fragment in a composition of 140 mM NaCl, 4 mM KCl, 20 mM Hepes, pH 7.4 (see page 29020 under (preparation of anti-GPVI Fab and F(ab')₂). While the prior art teachings may be silent as to the “induces an irreversible inactivation or degradation of a

Art Unit: 1644

collagen receptor on thrombocytes” per se; the antibody used in the reference is the same as the claimed antibody. Therefore “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” is considered inherent properties. As evidenced by Schulte et al that anti-GPVI agents, irrespective of their binding site may generally induce down-regulation of the receptor in vivo (see abstract in particular).

Since the office does not have a laboratory to test the reference antibodies, it is applicant’s burden to show that the reference antibody does not induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

15. Claims 1-2, 4 and 11-12 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Pat. No. 6,245,527, as is evidenced by Schulte et al (Blood, 15 May 2003, Vol. 101, No. 10, pp. 3948-3952).

The ‘527 patent teaches anti-GPVI antibodies that bind TANGO 268 and GPVI (TANGO 268 represents the platelet-expressed collagen receptor GPVI) (see col., 3, lines 1-6, col., 10, lines 65-67, col., 19, line 5 in particular). The ‘527 patent teaches anti-GPVI IgG antibody composition (see col., 19, line 27 in particular). The ‘527 patent further teaches that the GPVI/TANGO 268 modulators can be used to modulate thrombotic or hemorrhagic disorders, diseases exhibiting quantitative or qualitative platelet dysfunction and diseases displaying endothelial dysfunction such as coronary artery and cerebral artery diseases (see col. 22, lines 49-58 in particular). Furthermore, the ‘527 patent teaches a method to preparing monoclonal and polyclonal antibodies to GPVI/TANGO 268 (see col. 38 lines 12-59 in particular). Finally, The ‘527 patent teaches the preferred dosage of the antibodies is 0.1 mg/kg to 100 mg/kg of body weight (see col., 49, lines 22-25 in particular). While the prior art teachings may be silent as to the “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” per se; the antibody used in the reference is the same as the claimed antibody. Therefore “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” is considered inherent properties. As evidenced by Schulte et al that anti-GPVI agents, irrespective of their binding site may generally induce down-regulation of the receptor in vivo (see abstract in particular).

Since the office does not have a laboratory to test the reference antibodies, it is applicant’s burden to show that the reference antibody does not induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

Art Unit: 1644

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nieswandt *et al*, in view of Owens *et al* (1994) (IDS Ref. C58).

The teachings of Nieswandt *et al* reference have been discussed, *supra*.

The claimed invention differs from the reference teaching only by the recitation of a humanized antibody in claim 5.

Owens *et al* teach the modification of murine antibodies such as humanized antibody antibodies. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. (see the entire document).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the monoclonal antibody taught by Nieswandt *et al* as humanized antibody as taught by the Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are used in therapy of human diseases or disorders and much less likely to induce an immune response as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Art Unit: 1644

18. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nieswandt *et al*, Clemetson *et al* or US Pat. No. 6,245,527 each in view of U.S. Patent No. 6,406,888 (IDS Ref No. A).

The teachings of Nieswandt *et al*, Clemetson *et al* and the '527 patent have been discussed, *supra*.

The claimed invention differs from the reference teachings only by the recitation of a diagnostic agent comprising at least one labeled antibody chosen from a monoclonal antibody and a polyclonal antibody, wherein the at least one labeled antibody is directed against a GPVI epitope in claim 6

The '888 patent teaches antibodies that can be linked to other compounds, including therapeutic and diagnostic agents, using known methods to provide for targeting of those compounds to cells. For certain applications, including in vitro and in vivo diagnostic uses, it is advantageous to employ labeled antibodies. Suitable direct tags or labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent markers, chemiluminescent markers, magnetic particles and the like; indirect tags or labels may feature use of biotin-avidin or other complement/anti-complement pairs as intermediates (column 28, line 26-36 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to label the polyclonal antibody taught by Clemetson *et al*, the monoclonal antibody taught by Nieswandt *et al* or both the monoclonal and polyclonal antibodies taught by the '527 patent and use it as a diagnostic agent as taught by the '888 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because such labeled antibodies can be used in known methods for targeting specific compounds to cells.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clemetson *et al* (IDS ref No. 6) in view of Harlow (1989).

The teachings of Clemetson *et al* reference have been discussed, *supra*.

The claimed invention differs from the reference teaching only by the recitation of a method of producing a medicament against thrombotic diseases comprising providing at least one active principle, wherein the at least one active principle is a monoclonal antibody.

Art Unit: 1644

Harlow *et al* teach a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. fragments), harvesting spleen cells from said animal, fusing said spleen cells with myeloma cell line, and culturing said fused cells (i.e. hybridoma) under conditions that allow production of said antibody. Harlow *et al* further teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities (see pages 141-157 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce monoclonal antibody using the method taught by Harlow *et al* with the immunogenic fragment taught by Clemetson *et al*.

One ordinary skill in the art at the time the invention was made would have been motivated to do so because the monoclonal antibodies produced exhibit a high degree of specificity and great affinity as taught by Harlow.

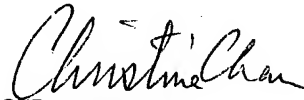
From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
November 12, 2004


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600